## REMARKS

This document is filed in reply to the office action dated April 1, 2004, which is identical to the office action dated January 4, 2004. In the January 4, 2004 office action, the Examiner mentioned a number of sequence alignments, but did not mailed them to Applicants' counsel. On March 24, 2004, Applicants' counsel conducted a telephone interview with the Examiner and requested the alignments. In the interview, the Examiner indicated that the alignments were indeed not mailed out. She subsequently mailed them to Applicants' counsel with the April 1, 2004 office action ("Office Action") and restarted the period for response.

In response to the Office Action, Applicants have (i) amended claims 1, 3, 6, and 8 to promote clarity, (ii) narrowed claim 15, and (iii) cancelled claims 16-22. Applicants have also added new claims 36-43. Support for "Escherichia coli open reading frame ECs3459" recited in claims 1 and 8 can be found at page 3, lines 5 of the specification.[1] Support for the new claims can be found at page 2, lines 1-5 of the Specification. No new matter has been introduced.

Claims 1-15 and 23-43 are pending. Claims 27-35 have been withdrawn from further consideration for being drawn to a non-elected invention. Claims 1-15, 23-26, and 36-43 are now under examination. Reconsideration of this application is requested in view of the following remarks:

### Objection to sequence listing

The Examiner objected to the sequence listing filed on April 9, 2002 for introducing new matter. See the Office Action, page 3, lines 8-9. The sequence listing included SEQ ID NOs: 1 and 2, which were based on nucleotides (nt) 81889-93238 of GenBank Accession No. AP002562. According to the Examiner, "access numbers in GenBank can be changed, thus introducing the possibility of new matter into the specification." She requested Applicants to provide (i) the region between nt 81889 and 93238 of GenBank Accession No. AP002562 as a

[1] Escherichia coli open reading frame ECs3459 corresponds to nt 82656-82862 of GenBank Accession No. AP002562. As it is flanked by SEQ ID NO: 1 (nt 82574-82591) or 3 (nt 82568-82591) and SEQ ID NO:2 (nt 83069-83052) or 4 (nt 83075-83052), a nucleic acid amplified from an Escherichia coli nucleic acid template with an upstream primer containing SEQ ID NO:1 or 3 and a downstream primer containing SEQ ID NO:2 or 4 inherently contains the Escherichia coli open reading frame ECs3459.

separate sequence in a substitute sequence listing (Exhibit A) and (ii) a verified statement that this separate sequence was the version of the nt 81889-93238 region at the time when the application was filed (Exhibit B).

At the Examiner's request, Applicants have filed herewith a substitute sequence listing and a verified statement. In view of these two documents, Applicants submit that the objection should be withdrawn.

Objection to claims 9 and 12

The Examiner objected to claims 9 and 12 under 37 CFR 1.75(c) "as being of improper dependent form for failing to further limit the subject matter of a previous claim." More specifically, the Examiner stated that the two claims, dependents of claim 8 and drawn to primers, "[have] no upper length limitation with regard to the primer, however, the claim [i.e., claim 8,] from which [claims 9 and 12] depended recite[s] an upper length limitation... therefore, claims 9 and 12 are broader than claim 8. " See the Office Action, page 4, lines 6-12.

Applicants note that, according to 37 CFR 1.75(c), "claims in dependent form shall be construed to include all the limitations of the claim incorporated by reference into the dependent claim." In other words, claims 9 and 12, which depend from claim 8, "shall be construed to include all the limitations of" claim 8, including the upper length limitation. For these reasons, Applicants submit that the Examiner's position is untenable and that the objection should be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-6 and 8-18 for failing to comply with the written description requirement on two grounds. Applicants will address each below:

I

The Examiner rejected claims 1-4 and 8-11 for containing new matter on the same ground that she asserted in the "Objection to the sequence listing" section above. See the Office Action, page 4, line 20 through page 5, line 10. For the same reasons set forth in that section, Applicants submit that the claims meet the written description requirement.

II

The Examiner rejected claims 1-3, 5-6, and 8-18 for failing to comply with the written description requirement. See the Office Action, page 5, lines 16-19.

Applicants have cancelled claims 16-18 and will discuss the other rejected claims, as well as new claims 36-43. Independent claim 8 is discussed first.

Independent claim 8 covers a nucleic acid amplified from an E. coli nucleic acid template with a pair of primers containing SEQ ID NOs: 1 or 3 and SEQ ID NO: 2 or 4, respectively. According to the Examiner, claim 8 does not meet the written description requirement since "[w]ith the exception of the recited SEQ ID NOs, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotide ..." See the Office Action, page 7, lines 4-6. Applicants have amended claim 8 to point out that the claimed nucleic acid contains E. coli open reading frame ECs3459, i.e., to include "a detailed chemical structure of the encompassed polynucleotide" in the claim.

The Examiner also stated that "SEQ ID NOs: 1-4 ... are found completely within the genome of [a] strain of Shigella in either accession number AE015280 or AE015281 ... therefore [the claimed nucleic acid] encompass[es] sequences from Shigella flexneri ...that have not been taught or described in the specification." See the Office Action, page 6, lines 6-13. Applicants would like to point out that, although the genome of Shigella flexneri contains SEQ ID NOs: 1-4, they do not flank a region containing the E. coli open reading frame ECs3459. Thus, they cannot be used to amplify a nucleic acid that contains this open reading frame as required in amended claim 8. Further, Applicants note that all of the 4 sequences are complementary to the same strand of the Shigella flexneri genome. As a pair of primers must be complementary to two different strands, respectively, so as to amplify a nucleic acid, the 4 sequences clearly cannot be used to amplify any nucleic acid from the Shigella flexneri genome. In other words, contrary to the Examiner's assertion, the claimed nucleic acid of claim 8 does not "encompass sequences from Shigella flexneri." Thus claim 8 meets the written description requirement.

Independent claim 1, as amended, covers a set of nucleic acids that include a pair of primers, which contain SEQ ID NO: 1 or 3 and SEQ ID NO: 2 or 4, respectively. These sequences can be used to generate, with an Escherichia coli nucleic acid as a template, a nucleic

acid containing the above-mentioned Escherichia coli open reading frame ECs3459. For the same reasons set forth above, claim 1 also meets the written description requirement.

Independent claim 15 has been amended to cover only a nucleic acid selected from the group consisting of SEQ ID NOs:5-8 and their complementary sequences. Applicants submit that this amendment has overcome the rejection.

Each of claims 2, 3, 5, 6, and 9-14, dependent from claim 1 or 8, recites a specific SEQ ID NO(s) or a nucleic acid length range. New claims 36-43, dependents from claim 1, recite a third nucleic acid containing a sequence selected from a group consisting of SEQ ID NOs:5-8 and their complements. In view of the above remarks, Applicants submit that these claims also comply with the written description requirement.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejected claims 1-26 for indefiniteness, contending that the length ranges of primers and probes recited in these claims are not clear. According to the Examiner,

> The claims recite primers that contain a specific SEQ ID NO: (SEQ ID NO[s]: 1-4): but the claims also recite that the primer can be a minimum of 18 nucleotides in length. The term "containing" stipulates that the full sequence is present in the larger sequence, however SEQ ID NOs:3 and 4 are each 24 nucleotides in length. Consequently, it is unclear how a sequence can "contain" either SEQ ID NO: 3 or 4 and be 18 nucleotides long. Further, the claims recite probes that contain specific SEQ ID NO: (SEQ ID NOs: 5-8) but also recite that the probe[s] can be a minimum of 26 nucleotides. The term "containing" stipulates that the full sequence is present in the larger sequence, however SEQ ID NOs[:] 5-7 are each 27 nucleotides in length. Consequently, it is unclear how a sequence can "contain" either SEQ ID NO: 5, 6, or 7 and be 26 nucleotides long. (See the Office Action, page 8, lines 6-15.)

Applicants disagree and would like to point out that "[w]hether a claim is invalid for indefiniteness depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the Specification." *North American Vaccine Inc. v. American Cyanmid Co.*, 28 USPQ2d 1333 (Fed. Cir. 1993).

Independent claims 1 and 8 recite primers that contain SEQ ID NO: 1, 2, 3, or 4. As taught in the specification, SEQ ID NOs: 1 and 2 are 18 nucleotides in length, and SEQ ID NOs: 3 and 4 are 24 nucleotides in length. In view of these teachings, those skilled in the art would clearly understand that (i) the primers containing SEQ ID NO: 1 or 2 are at least 18 nucleotides in length, and (ii) the primers containing SEQ ID NO: 3 or 4 are at least 24 nucleotides in length. In other words, 18 nucleotides are the minimal length of the primers containing SEQ ID NO: 1, 2, 3, or 4. Applicants therefore recite "18' as the lower limit of the length. Independent claim 15, as amended, is drawn to a group of probes consisting of SEQ ID NOs: 5-8 and their complements. The lengths of these probes are either 26 or 27 nucleotides. It is clear to those skilled in the art that the minimal length of a probe of this group is 26 nucleotides. Applicants therefore recite "26' as the lower limit of the length. As the length ranges for the recited primers or probes are clear, claims 1, 8, and 15 are definite. For the same reasons, all the claims depend from claim 1, 8, and 15 (i.e., claims 2-7, 9-14, and 23-26, as well as new claims 36-43)[2] are also definite.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejected claims 15-18, which recite SEQ ID NO: 5, 6, 7, or 8, for being anticipated by GenBank Accession Nos AF175847 and AX002476. See the Office Action, page 8, line 25 through page 9, line 15. On the other hand, she pointed out that claims drawn to a nucleic acid consisting of SEQ ID NO: 5, 6, 7, or 8 are free of prior art. See the Office Action, page 14, line 7.

Applicants have (i) amended claim 15 to limit the claimed nucleic acid to a group consisting of SEQ ID NOs: 5-8 and their complements, and (ii) cancelled claims 16-18. It is submitted that amended claim 15 is free of prior art. In other words, claim 15, as amended, is not anticipated by the two GenBank Accession Nos.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejected claims 1-3, 5, 6, and 8-18 for obviousness over GenBank Accession No. AE005490, GenBank Accession No. AE000346, GenBank Accession No.

[2] Claims 16-22 have been cancelled and therefore are not addressed.

Z70523, and GenBank Accession No. D90887, in view of Buck et al. Biotechniques, 1999, 27(3): 528-536 ("Buck"), U.S. Patent 5,374,718 to Hammond et al. ("Hammond"), U.S. Patent 5,693,769 to Hogan ("Hogan"), and Tijhie et al., J. Micobiol. Meth. Vol. 18, pp 137-150, 1993 ("Tijhie"). See the Office Action, page 10, lines 13-10.

Applicants respectfully traverse. As mentioned above, claims 16-18 have been cancelled, and claim 15, as amended, is free of prior art. Therefore, Applicants will only discuss claims 1-3, 5, 6, and 8-14, as well as new claims 36-43. Independent claim 1 is discussed first.

Claim 1 covers a set of nucleic acids that include a pair of primers, containing SEQ ID NO: 1 or 3 and SEQ ID NO: 2 or 4, respectively. It is the Examiner's position that (i) the above-mentioned 4 GenBank Accession Nos teach E. coli genomic sequences containing SEQ ID NOs: 1-4, but not any specific primers containing one of SEQ ID NOs 1-4, (ii) Hommond and Tijhie teach picking primers or probes for detection of Chlamydia pneumonia, (iii) Hogan teaches targeting sequences within the E. coli genome for detections of E. coli, and (iv) Buck teaches strategies for choosing primers. More specifically, the Examiner asserted that "Buck provides direct evidence that all primers [selected from a target sequence] would be expected to function ... every primer [selected from the just-mentioned four E. coli genomic sequences therefore] would have a reasonable expectation of success." See the Office Action, page 11, line 21 through page 12, line 2. She then concluded that it would be obvious for one skilled in the art to select a primer containing SEQ ID NO: 1, 2, 3, or 4 from the just-mentioned four E. coli genomic sequences based on the teachings of the four references.

Applicants disagree. Admittedly, the Buck reference describes a survey showing that 164 primers selected from a 300 bp target sequence functioned well in sequencing a template. However, "[the] template was pre-selected to contain a test sequence lacking obstacles to sequence extension and **purified** by double banding in CsCl-ethidium bromide isopycnic density gradients." The purification eliminates any potential non-specific annealings of the primers to contaminating sequences. In contrast, the nucleic acids of claim 1 can be used to amplify and detect **unpurified** E. coli sequences from samples, e.g., a specimen from a subject containing myriads of sequences (including those from the subject's genome). See, e.g., page 3, lines 1-2 and page 11, lines 10-18 of the specification. It is unreasonable to extrapolate data obtained on

an artificial and purified sequence to a natural and unpurified sequence. Thus, the Examiner's conclusion is untenable.

In view of the above reasons, Applicants submit that claim 1 is non-obviousness over the cited references. So are claims 2, 3, 5, 6, and 36-43, all of which depend from claim 1. Independent claim 8 is drawn to a nucleic acid obtained from amplification of an E. coli nucleic acid template with a pair of primers having, respectively, SEQ ID NO: 1 or 3 and SEQ ID NO: 2 or 4. Claims 9-14 depend from claim 8. For the same reasons set forth above, claims 8-14 are also non-obviousness over the cited references.

## CONCLUSION

Applicants submit that grounds for the rejections asserted by the Examiner have been overcome, and that claims, as pending, define subject matter that is free of new matter, sufficiently described, definite, novel, and non-obvious. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited. Please apply the additional claims fee of $18, as well as any other charges to deposit account 06-1050, referencing attorney docket 12674-005001.

Respectfully submitted,

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